WHAT IS CLAIMED IS:

1. A method of forming a compound of the general formula, Ar-R, the method comprising:

contacting a mixture of an aryl substrate with a nucleophilic leaving group, an organozinc species capable of transmetalation and a metal complex capable of effecting the coupling of an aryl substrate and an organozinc species to synthesize a compound of the formula Ar-R where Ar is an aryl or heteroaryl group and R is an aralkyl, arylmethyl or a (heteroaryl)methyl group.

2. A method of claim 3, wherein the metal complex is a nickel, palladium or platinum complex.

3. A method of forming a compound of the general formula, Ar-R, the method comprising the step of

contacting a mixture of aryl halide, ArX, and an organozinc species, RZnY, in the presence of at least a catalytic amount of a palladium complex under conditions conducive to the formation of an Ar-R bond, wherein:

Ar is optionally substituted phenyl, optionally substituted 1-naphthyl, optionally substituted 2-naphthyl, or optionally substituted heteroaryl having from 5 to about 18 ring atoms, 1 to about 3 rings and 1 to about 4 ring heteroatoms selected from N, O or S;

R is optionally substituted aralkyl;

X is Cl, Br, I, arylsulfonate, alkylsulfonate or triflate; and

Y is F, Cl, Br, I, arylsulfonate, alkylsulfonate or triflate.

4. A method of claim 3, wherein Ar-R bond formation is effected by a palladium mediated cross-coupling reaction.

5. A method of claim 3, wherein the mixture is dissolved in an inert solvent selected from hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, or oxygenated hydrocarbons.

6. A method of claim 3, wherein the mixture is dissolved in an inert solvent selected from diethyl ether, *tert*-butylmethylether, tetrahydrofuran, dioxane, dioxolane, benzene, toluene, ethylbenzene or xylenes;

7. A method of claim 3, wherein the mixture is dissolved in an inert solvent so the aryl halide, ArX, is present in about 0.01 M to about 2 M.

8. A method of claim 3, wherein the mixture is dissolved in an inert solvent so the aryl halide, ArX, is present in about 0.1M to about 1 M.

9. A method of any one of claims 3 to 8, wherein the mixture is heated to a temperature between about 25°C and about 150°C.

10. A method according to any one of claims 3 to 8, wherein the mixture is heated to a temperature between about 30°C and about 110 °C.

11. A method of any one of claims 3 to 8, wherein the mixture is heated to a temperature where the inert solvent refluxes.

12. A method of any one of claims 3 to 11, wherein formation of a cross-coupled product, Ar-R, occurs between about 1 minute and about 48 hours.

13. A method of any one of claims 3 to 11, wherein formation of a cross-coupled product, Ar-R, occurs between about 5 minutes and about 16 hours.

14. A method of any one of claims 3 to 11, wherein formation of a cross-coupled product, Ar-R, occurs between about 10 minutes and about 4 hours.

15. A method of any one of claims 3 to 14, wherein at least 50 mole % of Ar-X is converted into a cross-coupled product.

16. A method of any one of claims 3 to 14, wherein at least 75 mole % of Ar-X is converted into a cross-coupled product.

17. A method of any one of claims 3 to 14, wherein at least 90 mole % of Ar-X is converted into a cross-coupled product.

18. A method of any one of claims 3 to 14, wherein at least 95 mole % of Ar-X is converted into a cross-coupled product.

19. A method of claim 3, wherein the palladium catalyst is a L_2Pd complex which may comprise additional ligands bound to palladium, and L is phosphite or phosphite or L_2 taken in combination is chelating ligand selected from bis(phosphine), bis(phosphite), phosphine-phosphite or 2,2'-bipyridine derivative.

20. A method of claim 19, wherein L_2 is optionally substituted 1,1'-bis(diarylphosphino)-ferrocene, optionally substituted 2,2'-bis(diarylphosphino)-binaphthyl, optionally substituted 2,2'-bis(diarylphosphino)-biphenyl, optionally substituted α,ω- bis(diarylphosphino)-C_{1-6}alkylene, optionally substituted 1,2-bis(diC_{1-8}alkylphosphino)benzene, or 2,2'-bis(diarylphosphino)-diarylether.

21. A method of claim 19, wherein

L_2 is 1,1'-bis(diarylphosphino)-ferrocene, 2,2'-bis(diarylphosphino)-binaphthyl, or 2,2'-bis(diarylphosphino)-diphenylether; and

aryl is phenyl, 2-tolyl, 3-tolyl, or 4-tolyl.

22. A method of claim 19 wherein the palladium catalyst is selected from

L_2PdZ_2 precursor complexes where L is defined in claim 16 and Z is Cl, Br, or I;

or the palladium catalyst is generated *in situ* from a mixture of a palladium source selected from palladium chloride, palladium bromide, palladium acetate, L^*_nPd wherein

L^* is phosphine, amine, ether, thiophene, alkene, alkyne or a mixture thereof; and

and n is between about 2-4.

23. A method of claim 22, wherein the palladium catalyst is selected from L_2PdCl_2, L_2PdBr_2, and mixtures of $Pd(alkene)_n$ and L_2, a chelating bis(phosphine), wherein

alkene is selected from dibenzylidene acetone, norbornadiene, 1,5-cyclooctadiene, and ethylene such that 3 or 4 C=C bonds are coordinated to Pd; and

L_2 is selected from 1,1'-bis(diarylphosphino)-ferrocene, 2,2'-bis(diarylphosphino)-binaphthyl, or 2,2'-bis(diarylphosphino)-diphenylether.

24. A method of claim 23, wherein the mixture of $Pd(alkene)_n$ and L_2, a chelating bis(phosphine) has a molar ratio of Pd to L_2 between about 1:1 and about 1:3.

25. A method of claim 23, wherein the mixture of $Pd(alkene)_n$ and L_2, a chelating bis(phosphine) has a molar ratio of Pd to L_2 between about 1:1 and about 1:1.5.

26. A method of any one of claims 19 through 25, wherein the palladium catalyst loading is less than about 25 mole % relative to the Ar-X component.

27. A method of any one of claims 19 through 25, wherein the palladium catalyst loading is less than about 10 mole % relative to the Ar-X component.

28. A method of any one of claims 19 through 25, wherein the palladium catalyst loading is less than about 5 mole % relative to the Ar-X component.

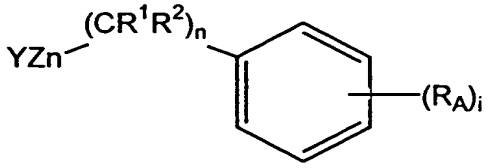
29. A method of any one of claims 19 through 25, wherein the palladium catalyst loading is less than about 2 mole % relative to the Ar-X component.

30. A method of claim 3, wherein the molar ratio of the Ar-X component to the RZnY component is between about 1:1 and about 1:10.

31. A method of claim 3, wherein the molar ratio of the Ar-X component to the RZnY component is between about 1:1.5 and about 1:5.

32. A method of claim 3, wherein the molar ratio of the Ar-X component to the RZnY component is between about 1:1.5 and about 1:3.

33. A method of claim 3, wherein RZnY is an organozinc compound of formula II:



II

wherein

Y is as defined in claim 3;

R^1 and R^2 are independently selected at each occurrence of R^1 and R^2 from the group consisting of hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, or C_{3-8}cycloalkyl;

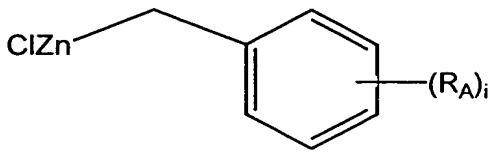
R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{1-6}alkoxy, chloro, fluoro, C_{1-4}fluoroalkyl, amino, mono and di(C_{1-6}alkyl)amino, nitrile, optionally substituted aryloxy, optionally substituted heteroaryloxy, C_{1-6}alkylthio, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aryl acetoxy or optionally substituted heteroaryl acetoxy; or

two R_A groups on adjacent ring atoms taken in combination form a second ring optionally comprising zero, one or two hetero ring atoms;

n is an integer from 1 to about 4; and

i is an integer from 0 to 5.

34. A method of claim 33, wherein RZnY is an organozinc compound of formula III:



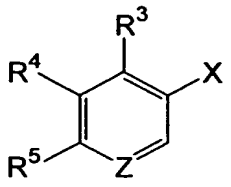
III

wherein:

R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, chloro, fluoro, C_{1-4}alkyl, C_{1-4}alkoxy, and C_{1-2}fluoroalkyl;

i is an integer from 0 to about 3.

35. A method of claim 3, wherein the aryl halide, ArX, is a compound of Formula IV:

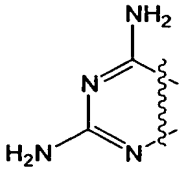


IV

wherein:

R^4 and R^5 are independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, chloro, fluoro, C_{1-6}fluoroalkyl, C_{1-6}alkoxy, amino, mono and di(C_{1-6}alkyl)amino, and nitrile; or

R^4 and R^5 taken in combination form a group of the formula:



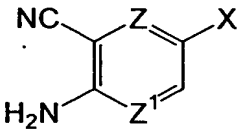
X is I or Br; and

Z is N or CR^3;

Z^1 is N or CH; and

R^3 is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, chloro, fluoro, C_{1-6}fluoroalkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, optionally substituted arylthio, or optionally substituted arylalkylthio.

36. A method of claim 35, wherein the aryl halide, ArX, is a compound of Formula V:



V

wherein:

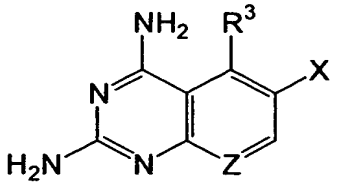
X is Br or I;

Z is N or CR^3;

Z^1 is N or CH; and

R^3 is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, chloro, fluoro, C_{1-6}fluoroalkyl, or C_{1-6}alkoxy.

37. A method of claim 35, wherein the aryl halide, ArX, is a compound of Formula VI:



VI

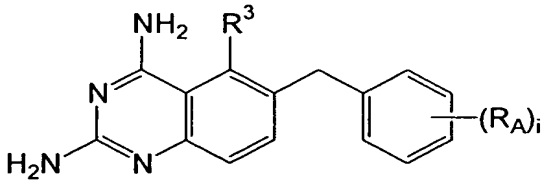
wherein:

X is Br or I;

Z is N or CH; and

R^3 is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, chloro, fluoro, C_{1-6}fluoroalkyl, or C_{1-6}alkoxy.

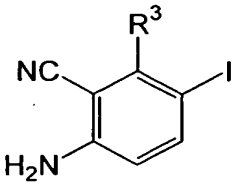
38. A method of forming a compound according to Formula I:



I

the method comprising the steps of

contacting an aryl halide of the formula:



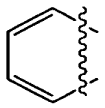
with at least one molar equivalent of a organozinc reagent, RZnY, and at least a catalytic amount of a palladium catalyst under conditions conducive to the formation of an C-C bond by a palladium mediated cross-coupling reaction;

contacting the product of the cross-coupling reaction with chloroformamidine under dry-fusion conditions conducive to formation of a compound according to Formula I, wherein

R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{1-6}alkoxy, chloro, fluoro, C_{1-4}fluoroalkyl, amino, mono and di(C_{1-6}alkyl)amino, nitrile, optionally substituted aryloxy, optionally substituted heteroaryloxy, C_{1-6}alkylthio, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aryl acetoxy or optionally substituted heteroaryl acetoxy; or

or

two adjacent R_A groups taken in combination form a group of the formula:

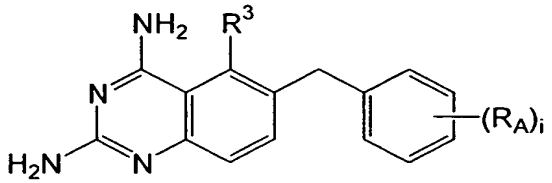


which may be optionally substituted;

R^3 is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, chloro, fluoro, C_{1-6}fluoroalkyl, or C_{1-6}alkoxy; and

Y is Cl, Br, I, or triflate.

39. A compound according to Formula I:

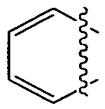


I

wherein:

R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{1-6}alkoxy, chloro, fluoro, C_{1-4}fluoroalkyl, amino, mono and di(C_{1-6}alkyl)amino, nitrile, optionally substituted aryloxy, optionally substituted heteroaryloxy, C_{1-6}alkylthio, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aryl acetoxy or optionally substituted heteroaryl acetoxy; or

two adjacent R_A groups taken in combination form a group of the formula:



which may be optionally substituted;

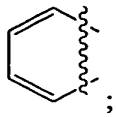
R^3 is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, chloro, fluoro, C_{1-6}fluoroalkyl, C_{1-6}alkoxy, C_{1-6}alkylthio, optionally substituted arylthio, or optionally substituted arylalkylthio; and

i is an integer from 0 to about 5.

40. A compound according to claim 39, wherein the compound is a lipophilic inhibitor of dihydrofolate reductase.

41. A compound of claim 39 wherein R_A is independently selected at each occurrence of R_A from the group consisting of hydrogen, chloro, fluoro, C_{1-4}alkyl, C_{1-4}alkoxy, and C_{1-2}fluoroalkyl; or

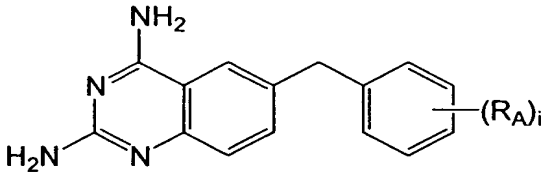
two adjacent R_A groups taken in combination form a group of the formula:


;

R^3 is hydrogen, methyl, chloro or fluoro; and

i is an integer from 0 to about 3.

42. A compound of claim 39 according to Formula I-A:

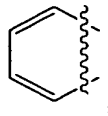


I-A

wherein

R_A is independently selected at each occurrence from the group consisting of hydrogen, fluoro, chloro, methoxy, methyl, and trifluoromethyl; or

two adjacent R_A groups taken in combination form a group of the formula:


;

i is an integer from 0 to about 3.

43. A pharmaceutical composition comprising a compound of any one of claims 39 through 42 and a pharmaceutically acceptable carrier.

44. A method for treating a mammal suffering or susceptible to a parasitic infection or disorder, comprising administering to the mammal an effective amount of a compound or composition of any one of claims 39 through 43.

45. A method of claim 44 wherein the mammal is immuno-compromised.

46. The method of claim 44 or claim 45, wherein the mammal is HIV-positive.

47. The method of any on of claims 44 through 46, wherein the mammal is suffering from an acquired immune deficiency disorder.

48. The method of claim 44, wherein the mammal is suffering from an autoimmune disorder or disease.

49. The method of any one of claims 44 through 48, wherein the mammal has a parasitic infection.

50. The method of claim 49, wherein the parasitic infection is a *Pneumocystis carinii* (Pc) and *Tozoplasma gondii* infection.

51. A method for treating an immuno-comprised mammal comprising administering to the mammal an effective amount of a compound or composition of any one of claims 39 through 43.

52. The method of claim 51, wherein the mammal is HIV-positive.

53. The method of claim 51, wherein the mammal has AIDS.

54. The method of claim 51, wherein the mammal has an autoimmune disorder.

55. The method of any one of claims 44 through 54 wherein the mammal is a human.